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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/596,783

02/08/2007

Laurence Hylton Patterson

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09/12/2008

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EXAMINER

CHANDRAKUMAR, NIZAL S

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

09/12/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/596,783	Applicant(s) PATTERSON ET AL.	
	Examiner NIZAL S. CHANDRAKUMAR	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16, 18-28 and 37-43 is/are pending in the application.
- 4a) Of the above claim(s) 20-29, 37-39 and 41-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16, 18, 19, 39, and 40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 07/28/2008 is acknowledged.

The traversal is on the ground(s) that

The Examiner seems to have misunderstood that the essential technical feature is that the anthraquinone compound of general formula I must have at least one cyclic amine group containing substituent and this in turn has a narrow meaning.

. This is not found

persuasive because, the pictured invariant structural moiety in all the groups is not a contribution over the prior art (see below rejections under 35 U.S.C. 103).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-16, 18-28, 37-43 are pending; 17, 30-36 are cancelled.

Elected Group I claims are 1-16, 18, 19, 39, and 40.

Claims 20-29, 37-39, 41-43 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/08/2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 18, 19, 39, 40 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for anthraquinone compounds with some of the substitution patterns claimed for formula I, does not reasonably provide enablement for the wide variety of combination and substitution patterns claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art. All of the factors have been considered with regard to the claim, with the most relevant factors discussed below:

The present invention relates to alkylaminoanthraquinones, with nitrogen containing heterocyclic substituents, as well as N-oxides of these compounds useful as anti-tumor agents. The claims are drawn to anthraquinone compounds in which all the possible 8-positions of the nucleus are

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optionally substituted with one or more substituted amino groups. The direction and working example provided in the specification is limited to making compounds that are limited to *the teachings in the prior art with respect to the substitution pattern* on the anthraquinone nucleus. As such, the synthetic method disclosed (nucleophilic substitution, dictated by addition-elimination mechanism) is enabling for compounds with limited substitution pattern. This limits that the formula (II) amine be positioned only at the peri positions, 1,4, 5 and 8 positions of the anthraquinone ring system. Further, any substituent (such as halogen, hydroxyl) already present in the precursor prior to the above-mentioned addition-elimination reaction protocol dictates the regiochemistry of the incoming amine of formula II. Furthermore, absent in specification is any disclosure with respect to making the regiospecifically positioned leaving group. There is no direction or guidance or working example or citations to alternate synthetic methods for securing the non-enabled possibilities. Thus there is no working example, direction or guidance for making compounds in which the critical amino group is in position 2,3, 6 or 7. Further there is no citation of commercial source or literature citation for procuring starting materials in lieu of working examples. It is also not seen, where in the specification enabling disclosure is found for making and or using compounds in which X2 is other than halogen or hydroxyl.

The claimed invention is not commensurate in scope with the breadth of enablement in as much as the working example in the application is limited compared to the wide breadth of the claims. Based on the teachings in the prior art and the disclosure in the specification, following limitations

R1 and R2 are at 1 or 4 positions and are H and/or -NHRoNR(5)2
R4 and R3 are at 5 or 8 positions and are H and/or OH
X2 is halogen or hydroxyl

to the claims would overcome this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

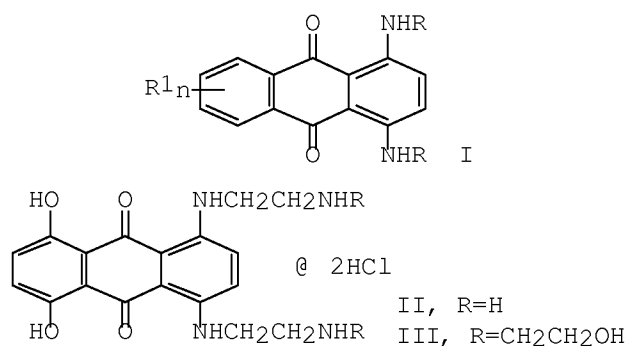
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-16, 18, 19, 39, 40 rejected under 35 U.S.C. 103(a) as being unpatentable over Murdock et al. (Journal of Medicinal Chemistry (1979), 22(9), 1024-30).

Murdock et al. teach anthraquinone anti-tumor compounds of the formulae



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Further, Murdock et al. teach compound III as having anti-tumor activity comparable to compounds in clinical trials (see page 1026, second paragraph, also see conclusionary remarks, page 1026, last paragraph, lines 1 and 2).

The difference between the anti-tumor compounds of the instant formula and those of the prior art is the substituents on the amino-containing groups in the above formulae. In the prior art, the amine contains straight alkylene chains and in the instant case the amine contains a cyclic amino group. Thus Murdock et al. do not teach compounds of the instant case which are drawn to formulae in which the amino containing R group has either a piperidine or pyrrolidine ring in place of the alkylene chain. Further Murdock et al. while teaching hydroxyl containing amino groups, do not teach halo (or other X₂) containing amino groups

However, one skilled in the art of medicinal chemistry would be motivated to make alternate forms of the prior art compound III, by cyclization of the alkylene chains because such structural modifications are routine in the art of design of analogs of known active molecules, further because of the knowledge in the art that cyclic ring structure, as found in anthraquinone adriamycin are not deleterious for the retention of anti-tumor activity. The instantly claimed compounds would have been suggested and thus obvious to one skilled in the art.

Prior art not relied upon:

Collier et al. Journal of Medicinal Chemistry (1988), 31(4), 847-857.

Agbandje et al. Journal of Medicinal Chemistry (1992, 35(8), 1418-1429.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/D. Margaret Seaman/
Primary Examiner, Art Unit 1625